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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/695,919	10/26/2000	Martin Gerl	02481.1704	4319

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EXAMINER	
CHEU, CHANGHWA J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 12/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/695,919	GERL ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 6-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 6-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claim 1-2, 6-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Iizuka et al. in view of Hara et al., Newgard et al. and Sedrani et al. (new reference, US 6635745).

Iizuka et al. teach measuring human C-peptide containing sample by mixing the sample a I^{125} C-peptide tracer, an antibody specific for the C-peptide containing sample, and a second antibody bead recognizing the first anti-C-peptide for determining the human C-peptide which is a degradation product from processing proinsulin. (See Abstract, Introduction, Materials and Methods; Table 1).

However, Iizuka et al. do not teach (1) using recombinant human insulin as the sample, (2) non-radioactive assay to determine the C-peptide in a sample; and (3) conducting the assay in a pH about 8.5 to 9.0.

Newgard teaches using genetic recombinant method to produce human insulin to meet the great demand and research in diabetes. (Col 3, line 20-45; Claim 1)

Hara et al. teach measuring human C-peptide using antibody recognition of C-peptide complex and conducted in a pH about 9.5 condition (See page 4, Section C).

Sedrani et al. teach using either radiolabel or chemiluminence label analyte tracer to measure the analyte in a sample by competing with the label tracer (Col. 13, line 55-65).

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to have provided the assay of Iizuka et al. to detect the C-peptide in a sample such as recombinant made insulin as taught by Newgard et al. because the great demand in medical field and C-peptide impurity is a common problem. Furthermore, it would have been obvious to one ordinary skill in the art at the time the invention was made to have provided Iizuka et al. with alternative labeled tracer, i.e. non-radioactive chemiluminescence as taught by Sedrain et al. to detect C-peptide and minimize radiocontamination and radiowaste disposal cost. Finally, with respect to pH level, it would have been obvious to one ordinary skill in the art at the time the invention was made to optimize the assay condition in the range of pH 9.0 as taught by Hara et al. in a similar art field, i.e. human C-peptide detection.

With respect to claim 6, both Iizuka and Hara et al. references teach antibodies recognizing human insulin C-peptide. Absence of evidence to the contrary, "human C-peptide" encompasses "reduced human insulin" or "alkyated human insulin" or "human insulin cleaved with endoproteinase".

With respect to claim 7, making antibody recognizing both C-peptide and preproinsulin with nearly the same affinity would have been obvious to one ordinary skill in the art under In re Aller because it has been held where general conditions of a claim are

disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. See In re Aller, 105 USPQ 233.

With respect to the feature of "the presence of about 1 mg/ml human insulin does not interfere with the binding of the antibody specific for C-peptide" in claim 10 and 15, both Iizuka et al. and Hara et al. do not explicitly disclose this feature, rather both references report detection limit of C-peptide about 0.1 ng/ml. Lack of evidence to the contrary, it would have been obvious to one artisan in the art to optimize assay, such as limit the interference at about 1 mg/ml without affecting antibody binding, since it merely involves routine practice in the art. In re Aller, 105 USPQ 233.

With respect to claim 11-12, using different animal, such as recited sheep instead of goat as taught by Iizuka et al, to generate antibody would have been obvious to one ordinary skill in the art because C-peptide is known and the antibody producing/isolation is well-practiced in the art.

2. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Iizuka et al, in view of Hara et al, Newgard et al., Sedrani et al., and further in view of Naithani et al.

Both references of Iizuka and Hara et al. references direct to human C-peptide whereas claim 13 recites using monkey C-peptide for the immunassay.

Naithani et al. teach monkey C-peptide synthesis and immunoassay study (See Abstract). Naithani et al. teach that both human and monkey C-peptide share substantial identity, e.g. only two amino acid difference (See Abstract). Naithani et al. suggest using monkey C-peptide for comparative immunoassay compared to human C-peptide. Supra.

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to have motivated Iizuka, Sedrani and Hara et al. to use monkey C-peptide as a comparative study as disclosed by Naithani et al. because it is known that

both monkey and human share substantial amino acid identity, and comparative animal study, particularly using species close to human, are favorable and often practiced in the art.

Response to Applicant's Arguments

3. Applicant's arguments with respect to claims 1-2, 6-15 have been considered but are moot in view of the new ground(s) of rejection.

4. The allowable subject matter indicated in the previous Office Action is hereby withdrawn in view of the new ground of rejection.

Conclusion

5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner
Art Unit 1641

November 9, 2005

LONG V. LE
SUPERVISORY PATENT EXAMINER
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11/09/05